Remarks/Arguments:

Applicant submits this Preliminary Amendment in association with a Request for Continued Examination (RCE) on said application. Applicant respectfully requests that the claim amendments made herein be entered in accordance with the filing of the RCE.

I. 35 U.S.C. § 112 second paragraph (Indefiniteness)

Claims 33, 34 and 44-47 are rejected under 35 USC 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner has rejected claim 33 as being incomplete, for omitting essential steps (i.e. a step that correlates the results of the *in vitro* inhibition assay of parts (a) and (b) with the determination of apoptosis in the neuronal tissue sample, parts (c) to (e)). To address this rejection, Applicant has added a step of correlating the results of the two studies, as suggested by the Office Action. In particular, claim 33 has been amended to recite in new step (f):

> "(f) correlating the results of steps (b) and (e) wherein a decrease in apoptosis in the neuronal tissue sample, when compared to apoptosis in a neuronal tissue sample from an animal not administered the compound, as determined in step (e), and a decrease in the presence or amount of the phosphorylated JNK substrate, when compared to incubating JNK with the JNK substrate absent the compound, as determined in step (b), taken together, correlate to the compound's ability to specifically inhibit JNK kinase activity in a mammal susceptible to or having a neurological condition."

Support for this amendment can be found throughout the application, and in particular, Example 2. In view of this amendment, applicant respectfully submits that the Examiner's concerns have been addressed and this rejection no longer applies. As such, Applicant respectfully request that the rejection of claims 33, 34 and 44-47 under 35 USC 112, second paragraph, be withdrawn.

II. 35 U.S.C. §102(e)

Claims 33, 34, 44 and 47 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,943,000 to Davis *et al* ("Davis et al."). In view of amended claim 33, Applicant respectfully traverses. Specifically, Applicant has amended claim 33 to

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now include the following limitations in step (a): "(a) incubating said compound in the presence of about 0.5 µg to about 2 µg of purified JNK and about 1 µg to about 3 µg of a JNK substrate ...". Support for this amendment can be found on page 15, lines 11-16 of the present application.

Davis et al. is drawn to *in vitro* and *in vivo* methods for screening inhibitors of JNK3 for diseases involving excitotoxicity. The Action suggests that Davis et al. meets the limitations of claim 33, parts a and b, because Davis et al. discloses incubating a test compound with a JNK and its substrate, wherein the degree of the phosphorylation of the JNK substrate is a measure of its ability to inhibit JNK. Applicant submits, however, that Davis et al. merely suggest this procedure as one of many possible alternative assays that can be used to identify compounds that interact with JNK3. Davis et al., however, do not disclose any detail on the quantity or amounts of either JNK or JNK substrate that are incubated with test compound. Further, there is no mention in Davis et al. of the use of purified JNK for such screening purposes. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Because Davis et al. do not expressly nor inherently describe any quantities or amounts of JNK or JNK substrate, nor the use of purified JNK, Davis et al. does not anticipate the claimed invention.

In view of the position set forth above, Applicant respectfully requests that rejection of claims 33, 34, 44 and 47 under 35 U.S.C. § 102(e) as anticipated by Davis et al. be withdrawn.

III. 35 U.S.C. § 103 (Park et al. in view of Davis et al.)

Claims 33, 44 and 47 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Park *et al.* (U.S. 6,087,366) in view of Davis *et al* (U.S. 6,943,000). Applicant respectfully traverses.

The Action suggests that Park et al. teach all of the elements of the rejected claims, except that Park et al. do not disclose that the test compound's ability to inhibit neuronal apoptosis was determined by administering the compound to an animal, harvesting neuronal

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tissue from said mammal, determining apoptosis in the tissue sample compared to a baseline sample to determine the compound's ability to specifically inhibit JNK in the mammal. The Action then brings in Davis et al. to remedy this problem, and argues that it would have been obvious to assess the ability of a compound to specifically inhibit JNK activity in a mammal by performing the in vitro assay with isolated JNK taught by Park et al. and correlating it with the TUNEL methodology taught by Davis et al. Applicant submits that such a leap is not suggested or motivated by the Park et al. reference.

Park et al. use a well known c-Jun kinase *in vitro* assay merely as an investigative tool to better understand the mechanism of action of flavopridol and olomoucine. Initially, there is no mention in Park et al. of a comparison of the *in vitro* kinase data of JNK incubated with a compound versus that not incubated with a compound as required by the claims. there is no desire or motivation expressed by Park et al. to correlate the *in vitro* phosphorylation results with *in vivo* apoptosis results because Park et al. has already determined its positive *in vivo* data prior to the c-Jun kinase activity detection step. In fact, Park et al. teach away from incorporating a correlation step because the compounds of Park et al. did not even show inhibition of JNK kinase activity. As stated in Park et al. (and noted by the Action), the "observations indicate that it is unlikely that the CDK inhibitors used here promote survival by preventing activation of JNK and that at least flavoprinol does not work by inhibiting JNK activity." (Column 10, lines 34-38). As such, the rejection is insufficient for failure to provide specific factual findings for motivation to combine these references. Moreover, the motivation suggested by the Action (i.e. the *in vivo* is better) is not an appropriate motivation to achieve the claimed invention which instead uses sequential *in vitro* and *in vivo* testing. In fact, Park et al. may even be viewed as suggesting to a skilled artisan that one could go directly to *in vivo* testing. It is therefore Applicant's position that there is no motivation or desire expressed by Park et al. to look to Davis et al. to supply the missing elements of the present claims, and, as such, there is no proper motivation to make the combination.

In view of the above, Applicant respectfully requests that the rejection of claims 33, 44 and 47 under 35 U.S.C. § 103(a) as being unpatentable over Park *et al.* in view of Davis *et al* be withdrawn.

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IV. 35 U.S.C. § 103 (Park et al. in view of Davis et al., in further view of Liu)

Claims 33, 44, 46 and 47 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Park *et al.* (U.S. 6,087,366) ("Park") in view of Davis *et al* (U.S. 6,943,000) ("Davis"), as applied to claims 33, 44 and 47, in further view of Liu (1997; cited in the Office Action mailed on 6/14/05). Applicant respectfully traverses.

For the reasons set forth above, there is no proper motivation to combine Park et al. with Davis et al., and, as such, this rejection cannot stand for that reason alone. As such, Applicant respectfully requests that the rejection of claims 33, 44, 46 and 47 under 35 U.S.C. § 103(a) as being unpatentable over Park *et al.* in view of Davis *et al* , and in further view of Liu, be withdrawn.

V. 35 U.S.C. § 103 (Davis et al. in view of Liu)

Claims 33, 34, 44, 46 and 47 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Davis *et al* (U.S. 6,943,000) ("Davis") as applied to claims 33, 34, 44 and 47, in view of Liu (1997; cited in the Office Action mailed on 6/14/05). Applicant respectfully traverses.

As set forth in the arguments presented above, Davis et al. does not anticipate the elements of the claimed invention that it is cited for in this rejection. Further, Liu et al. do not supply the missing elements. As such, this rejection cannot stand. Applicant therefore respectfully requests that the rejection of claims 33, 34, 44, 46 and 47 under 35 U.S.C. § 103(a) as being unpatentable over Davis *et al* in view of Liu, be withdrawn.

VI. 35 U.S.C. § 103 (Park et al. in view of Davis et al., in further view of Gnegy et al.)

Claims 33, 44, 45 and 47 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Park *et al.* (U.S. 6,087,366) ("Park") in view of Davis *et al* (U.S. 6,943,000) ("Davis"), as applied to claims 33, 44 and 47, in further view of Gnegy *et al.* (1976, "Gnegy"). Applicant respectfully traverses.

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For the reasons set forth above, the motivation to combine Park et al. and Davis et al. is improper, and, as such, this rejection cannot stand for that reason alone. As such, Applicant respectfully requests that the rejection of claims 33, 44, 45 and 47 under 35 U.S.C. § 103(a) as being unpatentable over Park *et al.* in view of Davis *et al* , and in further view of Gnegy *et al.*, be withdrawn.

VII. 35 U.S.C. § 103 (Davis et al. in view of Gnegy et al.)

Claims 33, 34, 44, 45 and 47 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Davis *et al* (U.S. 6,943,000) ("Davis"), as applied to claims 33, 34, 44 and 47, in view of Gnegy *et al.* (1976, "Gnegy"). Applicant respectfully traverses.

As set forth in the arguments presented above, Davis et al. does not anticipate the elements of the claimed invention that it is cited for in this rejection. Applicant therefore respectfully requests that the rejection of claims 33, 34, 44, 45 and 47 under 35 U.S.C. § 103(a) as being unpatentable over Davis *et al* in view of Gnegy *et al.*, be withdrawn.

Conclusion

The foregoing is believed to be fully responsive to the office action dated February 2, 2006. The embodiments presented are believed to be allowable over the prior art of record. Consideration and allowance of the claims is respectfully requested.

If the Examiner believes that a telephone conference with Applicants' attorneys would be advantageous to the disposition of this case, the Examiner is cordially requested to telephone the undersigned. If the Examiner has any questions in connection with this paper, or otherwise if it would facilitate the examination of this application, please call the undersigned at the telephone number below.

Applicant believes that a three-month extension of time is required for entry of the current response and hereby respectfully petitions the Commissioner for a three-month extension. Therefore, pursuant to 37 C.F.R. §1.136(a), please accept this as authorization to

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charge the **Deposit Account No. 50-3570** in the amount of **$1,020.00** for a three-month extension under 37 C.F.R. §1.17(a)(1). In the event that any fee has been inadvertently overlooked and is required, the Commissioner is hereby authorized to charge any required fee or credit any overpayment to **Deposit Account No. 50-3570**.

Respectfully submitted,

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Dated: August 1, 2006

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